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EXAMINER	
LIU, SAMUEL W	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 10/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/684,215	SKEIKY ET AL.	
	Examiner	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication app ars on the cover sheet with th corr spondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,10,11,13-16,27-29 and 31-38* is/are pending in the application.

4a) Of the above claim(s) *none* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,10,11,13-16, 27-29 and 31-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The response filed 18 August 2003, which amends claims 1-3, 6, 10-11, 13 and 27, and adds claims 32-38 has been entered (note that claims 7-9, 12, 17-26 and 30 are previously cancelled by applicants). The following Office action is applicable to pending claims 1-6, 10-11, 13-16, 27-29 and 31-38.

The grounds of objection and/or rejection not explicitly stated and/or set forth below are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, 27-29, 31 and 34-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is unclear as to the recitation "WT 1" because "WT" stands for dipeptide sequence "Trp-Thr"; does the disclosed nucleic acid molecule encode this peptide ?

Claim 27 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, e.g., isolating or/and identifying the expressed fusion polypeptide. See MPEP § 2172.01. Note that the claimed method for producing a fusion protein comprising only the step of expressing a recombinant polynucleotide encoding the fusion polypeptide is insufficient for producing the protein thereof because producing mRNA for the polypeptide is

also a consequence of expression of a recombinant polynucleotide (a gene). The dependent claims are also rejected.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The followings are the new grounds of rejection

The claims 1, 3-4, 10, 13, 27-29, 31-32, 34 and 36-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Reed S. G. et al. (WO 9709429).

Reed *et al.* teach the TbRa12 polynucleotide (see page 6, line 29) of *the patent* SEQ ID NO:4 (see pages 49-50) wherein nucleotides 11-406 of the patent SEQ ID NO:4 encodes the amino acid sequence of SEQ ID NO:67 (total residues: 1-132, see page 103) that is identical to SEQ ID NO:4 polypeptide (residues 1-132) of the instant application. Note that the above-mentioned nucleotide sequence reads on SEQ ID NO:3 of the instant application. Reed et al. teach the polynucleotide encoding a fusion protein which comprises two sequences (see the patent claims 3, 5 and 42, and page 5, lines 7-9), and teach that the antigenic polypeptide (e.g., SEQ ID N:67) is linked to non-*Mycobacterium tuberculosis* sequence (e.g., poly-His or an immunoglobulin Fc region, see page 12, lines 1-4). Also, Reed et al. teach the fusion partner in the recombinant sequence encompasses non-*Mycobacterium tuberculosis* sequence (i.e., heterologous sequence, see page 10, lines 32-33). The above Reed et al. teachings meet the

limitations set forth in claims 1, 13 and 32 of the instant application. Since Reed et al. teach the peptide linker is engineered between fusion partner sequences (see page 17, line 27 to page 18, line 4), the Reed's patent anticipates claim 3 of the current application.

Reed et al. teach the above-mentioned recombinant polynucleotide comprising the sequence encoding a Ra12 fragment (nucleotides 11-100) that encodes amino acid sequence of the instant SEQ ID NO:17, which meets the limitation set forth in claim 10 of the current application. Note that claim 10 recites "the recombinant nucleic acid comprising a ..." wherein the recitation "comprising" is open language as opposed to "consisting of").

Further, Reed et al. teach a method of producing the fusion polypeptide comprising expressing in a host-vector expression system a polynucleotide fusion construct (see page 14, lines 14-19) wherein (i) the host cell is *E.coli.* (see the patent claims 6-8 and page 14, line 27-29), and (ii) there is a linker peptide located between the first and the second fusion sequence (see page 17, line 27 to page 18, line 4), as applied to the application claims 27-29, 31, 34 and 36. Since Reed et al. teach the Ra12 sequence which reads on the application SEQ ID NO:17, the Reed at l. teaching also anticipates claim 37 of the current application.

Therefore, Reed et al. anticipate 1, 3-4, 10, 13, 27-29, 31-32, 34 and 36 of the instant application.

Claims 1, 3, 10, 13, 27-29, 31-32, 34 and 36-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Reed S. G. et al. (WO 9709428).

Reed *et al.* teach the TbRa12 polynucleotide, i.e., the *application* SEQ ID NO:3, (see page 6, line 12) which encodes *the patent* polypeptide SEQ ID NO:4 (see page 50); the TbRa12 polynucleotide encodes the polypeptide of SEQ ID NO:66 consisting of 132 amino acid residues (see page 8, line 14 and pages 96-97) that is identical to SEQ ID NO:4 polypeptide of the instant application. Reed et al. teach that the polynucleotide encoding a fusion protein comprises two sequences wherein the second fusion partner is an antigenic polypeptide (see page 5, lines 6-9). Reed et al. also teach the polypeptide (SEQ ID NO:66) is linked to non-*Mycobacterium tuberculosis* sequence (e.g., poly-His or an immunoglobulin Fc region, see page 12, lines 9-12). The above Reed et al. teachings are thus meets the limitations set forth in claims 1, 13 and 32 of the instant application. Since Reed et al. teach the peptide linker is engineered between fusion partner sequences (see page 21, lines 12-13), the Reed at al. teaching also anticipates claim 3 of the current application.

Reed et al. teach a recombinant polynucleotide comprising the sequence encoding a Ra12 sequence consisting of the application sequence of SEQ ID NO:17 (see nucleotides 11-100). Since claim 10 recites "the recombinant nucleic acid comprising a ..." wherein the recitation "comprising" is open language as opposed to "consisting of", the Reed et al. teaching also anticipates the application claim 10. Since Reed et al. teach the Ra12 sequence which reads on the application SEQ ID NO:17, the Reed et al. teaching also anticipates claim 37 of the current application.

Further, Reed et al. teach a method of producing the fusion polypeptide comprising expressing in a host cell a polynucleotide fusion construct (see page 18) wherein (i) the host cell is *E.coli.* (see the patent claims 5-7 and page 18, line 17), (ii) the fusion construct is operably

linked to transcriptional regulatory element (e.g., promoter, see page 22, lines 9-14), and (iii) there is a linker peptide located between the first and the second fusion sequence (see page 21, lines 12-13), as applied to the application claims 27-29, 34 and 36.

Therefore, Reed et al. anticipate 1, 3, 10, 13, 27-29, 31-32, 34 and 36 of the instant application.

Claim Rejections - 35 USC §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 10-11, 13-16, 27-29, 31-36 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reed, S. G. et al. (WO 9709428) taken with Wang T. et al. (US Pat. No. 6509448).

Reed *et al.* teach the TbRa12 polynucleotide, i.e., the *application* SEQ ID NO:3, (see page 6, line 12) which encodes *the patent* polypeptide SEQ ID NO:4 (see page 50); the TbRa12 polynucleotide encodes the polypeptide of SEQ ID NO:66 consisting of 132 amino acid residues

(see page 8, line 14 and pages 96-97) that is identical to SEQ ID NO:4 polypeptide of the instant application. Reed et al. teach that the polynucleotide encoding a fusion protein comprises two sequences wherein the second fusion partner is an antigenic polypeptide (see page 5, lines 6-9). Reed et al. also teach the polypeptide (SEQ ID NO:66) is linked to non-*Mycobacterium tuberculosis* sequence (e.g., poly-His or an immunoglobulin Fc region, see page 12, lines 9-12). The above Reed et al. teachings are applicable to claims 1, 13 and 32 of the instant application.

Reed et al. teach the peptide linker is engineered between fusion partner sequences (see page 21, lines 12-13), as applied to claim 3 of the current application.

Reed et al. teach a recombinant polynucleotide comprising the sequence encoding a Ra12 sequence consisting of the application sequence of SEQ ID NO:17 (see nucleotides 11-100). Since claim 10 recites "the recombinant nucleic acid comprising a ..." wherein the recitation "comprising" is open language as opposed to "consisting of", the Reed et al. teaching is applicable to the application claim 10.

Further, Reed et al. teach a method of producing the fusion polypeptide comprising expressing in a host cell a polynucleotide fusion construct (see page 18) wherein (i) the host cell is *E.coli.* (see the patent claims 5-7 and page 18, line 17), (ii) the fusion construct is operably linked to transcriptional regulatory element (e.g., promoter, see page 22, lines 9-14), and (iii) there is a linker peptide located between the first and the second fusion sequence (see page 21, lines 12-13), as applied to the application claims 27-29, 31, 34 and 36.

Reed et al. does not explicitly teach that Ra12 polynucleotide is linked 5' to non-*M. tuberculosis* sequence and that the peptide liker which connects the fusion partners contains a cleavage site and the expression vector system thereof.

Wang et al. teach the immunological fusion partner, e.g., Ra12 polypeptide, is 5' to the subject polypeptide (see the patent SEQ ID NO: 1864 which *comprises* (i) Ra12 sequence (residues 8 to 135) which reads on the application SEQ ID NO:18, and (ii) non-*M. tuberculosis* sequence (residues 138 to 273) which is a eukaryotic sequence (see column 101, lines 48-51), as applied to claims 2, 11, 33 and 38 of the instant application.

Wang et al. teach that the peptide linker is employed to separate the first and second fuses polypeptide components wherein the peptide linker contain a cleavage site (column 68, lines 51-55), as applied to claims 3-4 of the current application.

Wang et al. teach an affinity tag, e.g., the fusion protein contains 6-His tag for facilitating purification of the expressed fusion polypeptide (see column 73, lines 1-15), as applied to claim 5 of the instant application.

Further, Wang et al. teach the host-expression vector system comprising the fusion construct has a promoter operably linked to the recombinant polynucleotide (see column 91, lines 55-65, and Example 10), wherein the host cell is *E.coli.* (see Example 10), as applied to claims 14-16 of the current application.

It would have been obvious to one of ordinary skill in the art at the time the invention was made would have combined the teachings of the above references because Reed et al. teach TaRa12 fusion and a method of producing the fusion molecule thereof, and Wang et al. teach the

fusion partner (non-*M. tuberculosis*) to the Ra12 sequence, the peptide linker containing a cleavage site, and a expression vector system for the fusion molecule thereof.

When combined, there would have been the following advantages: (1) Ra12 composition comprising the immunological fusion partner derived from *Mycobacterium tuberculosis* is used in enhancing the expression and/or immunogenicity of heterologous polynucleotide/polypeptide; as taught by Wang et al. (see column 53, lines 17-23), and (2) peptide linker sequence is employed to separate the first and second fusion partners by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Thus, it would have been obvious to the skilled artisan to combine the above reference teachings to obtain heterologous polypeptide of interest comprising the Ra12 sequence and develop a method of producing such fusion polypeptide in stable form and high yield.

Given the above motivation one of ordinary skill in the art would have combined the teachings of the above references to produce the Ra12 fusion molecules comprising Ra12 sequence, non- *M. tuberculosis* sequence, the peptide linker containing a cleavage suite and affinity tag sequence for facilitating purification of the fusion products. Therefore, the claimed invention was *prima facie* obvious to make and use the invention at the time it was made.

Claim Rejections - Provisional Rejection, Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed.

Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130 (b). Effective 1 January 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 11 and 14-15 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-4 and 7 of copending Application No. 09780669. This is a provisional double patenting rejection because the conflicting claims have not in fact been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows:

Claim 1 of Application 09780669 discloses an isolated polynucleotide of SEQ ID NO: 822 which is a fusion construct: Ra12-P510S-C (see [0601]) wherein P510S-C is a mammalian polynucleotide, i.e., non-*Mycobacterium tuberculosis* molecule (see [0935] and [0044]) and wherein the Ra12 sequence (nucleotides: 22-405) of SEQ ID NO:822 encodes the polypeptide identical to SEQ ID NO: 18 of the current invention and the Ra12 sequence is located 5' to the

P510S-C sequence; and claim 2 and 7 of 09780669 set forth that P510S-C amino acid sequence of SEQ ID NO:826 (see [0605] and the patent claim 2) is a component of a fusion protein (see the patent claims 2 and 7). Thus, the 09780669 disclosure is an obvious variation of claims 1-2 and 11 of the current application.

Claims 3 and 4 of 09780699 set forth an expression vector comprising the above-mentioned polynucleotide operably linked to an expression control sequence (i.e., transcriptional regulatory element, see [0709]) and a host cell into which the expression vector is transferred. Claims 3 and 4 of 09706999 and the instant claims 14 and 15 disclose the common subject matter.

It is therefore concluded that the claims of the present application are not patentably distinct from the claims of Application No. 09780669.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is (703) 306-3483. The examiner can normally be reached from 9:00 a.m. to 5:30 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 703-308-2923. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

Art Unit: 1653

SWL

Samuel Wei Liu, Ph.D.

October 14, 2003

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER